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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/908,950	GETTS ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 July 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 07, 2007 has been entered.

Status of the Application

2. The action is in response to the RCE filed on February 07, 2007. Claims 1-56 are currently pending. All arguments and amendment have been fully considered and thoroughly reviewed and deemed unpersuasive for the reasons that follow. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Sequence Rules and Objection to the Specification

3. The specification is objected because of the following informalities:

(i) This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply the requirements of 37 CFR 1.821 through 1.825.

The instant application recites sequences that are not identified by SEQ ID No. (see at least Fig. 2 reciting a sequence of 12 nucleotides) recite a nucleic acid sequence / amino acid sequence with more than 10 nucleotides or 4 amino acids, which is not identified by SEQ ID NO.). Examiner also notes that the application contains no sequence listing either in the form of a paper copy or in a computer readable form. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 47-51, 57-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 47-51, 57-58 provides for the use of an array, a first component, a second component, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 47-51, 57-58 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 1-3, 7-8, 17, 19-21, 22, 25-26, 36, 39-54, 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dellinger et al. (USPN. 5, 853,993) in view of Barbera-Guillem et al. (US 6,261,779).

Dellinger et al. teach a method of claims 1, 47, for determining the presence or absence of a specific nucleic acid sequence in an RNA reagent of a target sample, said method comprises (a) incubating a mixture comprising (i) a first component including an RNA reagent (mRNA) extracted from a target sample, said RNA reagent having a target nucleic acid sequence and a capture sequence (homopolymeric tail) (see col. 4, line 41-43, col. 5, line 4-7); (ii) a second component comprising a capture reagent (reporter probe) comprising a label capable of emitting a detectable signal and a nucleotide sequence complementary to the capture sequence of the RNA reagent of the first component (see col. 4, line 44-45, col. 5, line 7-12, line 23-46), at a first temperature to induce hybridization and thereby to form a pre-hybridized RNA-capture reagent complex (reporter-analyte complex (see col. 5, line 34-46); (b) contacting pre-hybridized RNA-Capture complex with a microarray having thereon a plurality of features each comprising a

particular probe nucleotide sequence (immobilized capture probe) (see col. 4, line 44-46); (d) incubating said mixture at a second temperature to induce hybridization between pre-hybridized RNA-capture reagent complex and the probe on the array, and detecting the he hybridization pattern (col. 4, line 46-49, col. 7, line 27-58).

With regard to claim 2, 20, 49, Dellinger et al. teach that the capture reagent includes carbohydrates, proteins and nucleic acids (see col. 3, line 32-37, col. 8, line 60-62);

Dellinger et al. teach a method of claims 3, 44, for determining the presence or absence of a specific nucleic acid sequence in an RNA reagent of a target sample, said method comprises (a) incubating a mixture comprising (i) a first component including an RNA reagent (mRNA) extracted from a target sample, said RNA reagent having a target nucleic acid sequence and a capture sequence (homopolymeric tail) (see col. 4, line 41-43, col. 5, line 4-7); (ii) a second component comprising a capture reagent (reporter probe) comprising a label capable of emitting a detectable signal and a nucleotide sequence complementary to the capture sequence of the RNA reagent of the first component (see col. 4, line 44-45, col. 5, line 7-12, line 23-46), at a first temperature to induce hybridization and thereby to form a pre-hybridized RNA-capture reagent complex (reporter-analyte complex (see col. 5, line 34-46); (b) contacting pre-hybridized RNA-capture complex with a microarray having thereon a plurality of features each comprising a particular probe nucleotide sequence (immobilized capture probe) (see col. 4, line 44-46); (d) incubating said mixture at a second temperature to induce hybridization between pre-hybridized RNA-capture reagent complex and the probe on the array, and detecting the he hybridization pattern (col. 4, line 46-49, col. 7, line 27-58).

With regard to claims 17, 22, 36, Dellinger et al. teach said method further comprises passing a base solution to separate the hybridized sequences from the unhybridized probe sequences or a wash step (see col. 6, line 17-27, col. 9, line 43-45, col. 10, line 51-60);

With regard to claim 7-8, 25-26, 50-51, 56, Dellinger et al. teach that the capture sequence is a single-stranded oligonucleotide consisting of at least one adenine base or at least one thymine base (polyA tail or dT tail) (see col. col. 5, line 23-67, col. 6, line 1, line 49-67, col. 7, line 1-4);

With regard to claim 19, Dellinger et al. teach a method for determining the presence of a specific sequence in a RNA reagent of a target sample, said method comprising (a) contacting a first component including an RNA reagent extracted from a target sample, said RNA reagent having a target nucleic acid sequence and a capture sequence (homopolymeric tail) (see col. 4, line 41-43, col. 5, line 4-7) with a microarray having a plurality of features each comprising a particular probe nucleotide sequence (immobilized capture probe) (see col. 6, line 17-21); (b) incubating the RNA reagent and the complementary probe nucleic acid sequences on a microarray at a first temperature to hybridize the target nucleotide sequence of the RNA reagent to the complementary probe on the microarray (to form a capture probe-analyte hybrid, see col. 6, line 17-21); (c) contacting a second component comprising a capture reagent comprising a label and a nucleotide complementary to the capture sequence of the RNA reagent of the first component and (d) incubating at a second temperature to induce hybridization between the first and second component , wherein the hybridization signal is detected (see col. 6, line 21-27).

With regard to claim 21, 46, Dellinger et al. teach a method for determining the presence of a specific sequence in a RNA reagent of a target sample, said method comprising (a)

contacting a first component including an RNA reagent extracted from a target sample, said RNA reagent having a target nucleic acid sequence and a capture sequence (homopolymeric tail) (see col. 4, line 41-43, col. 5, line 4-7) with a microarray having a plurality of features each comprising a particular probe nucleotide sequence (immobilized capture probe) (see col. 6, line 17-21); (b) incubating the RNA reagent and the complementary probe nucleic acid sequences on a microarray at a first temperature to hybridize the target nucleotide sequence of the RNA reagent to the complementary probe on the microarray (to form a capture probe-analyte hybrid, see col. 6, line 17-21); (c) contacting a second component comprising a capture reagent comprising a label and a nucleotide complementary to the capture sequence of the RNA reagent of the first component and (d) incubating at a second temperature to induce hybridization between the first and second component , wherein the hybridization signal is detected (see col. 6, line 21-27).

With regard to claims 39- 42, Dellinger et al. teach that said probe nucleotide is an oligonucleotide (oligonucleotide sequence, which includes RNA and DNA sequences) (see col. 3, line 6-31);

With regard to claim 43, 45, Dellinger et al. teach that the second component comprises a capture reagent having at least one arm comprising said label and at least one second arm comprising said nucleotide sequence complementary to said capture sequence of the RNA reagent (see col. 8, line 64-67, col. 9, line 1-19, indicates hairpin structures comprise two arms one having a label and other having complementary sequence with a target analyte).

With regard to claim 46, 48, Dellinger et al. teach that the second component comprises a capture reagent having at least one arm comprising said label and at least one second arm

comprising said nucleotide sequence complementary to said capture sequence of the RNA reagent (see col. 8, line 64-67, col. 9, line 1-19, indicates hairpin structures comprise two arms one having a label and other having complementary sequence with a target analyte).

With regard to claim 52, Dellinger et al. teach a kit composition comprising (a and b) an array of probe sequences and RNA reagent comprising capture sequence (homopolymeric regions (see col. 2, line 27-32), immobilized capture probe sequences on a solid surface is considered as a microarray); (c) a second component (reporter probe) comprising a complementary nucleotide sequence to said capture sequence on the RNA reagent (analyte homoplymeric region) and said second component further comprises a label (see col. 2, line 30-32, col. 3, line 32-37).

With regard to claim 53, Dellinger et al. teach a kit composition comprising (a and b) an array of probe sequences and RNA reagent comprising capture sequence (homopolymeric regions (see col. 2, line 27-32), immobilized capture probe sequences on a solid surface is considered as a microarray); (c) a second component (reporter probe) comprising a complementary nucleotide sequence to said capture sequence on the RNA reagent (analyte homoplymeric region) and said second component further comprises a label (see col. 2, line 30-32, col. 3, line 32-37).

With regard to claim 54, Dellinger et al. also each that the second component (reporter probe) comprises molecules selected from the group of carbohydrates, proteins and nucleic acids (see col.8, line 60-63);

With regard to claims 7, 25, 51, 56, Dellinger et al. teach said capture sequence (homopolymeric region) comprises poly A tail (see col. 5, line 49-67, col. 6, line 15).

However, Dellinger et al. did not teach use of a second component comprising capture reagent with multiple first arms and multiple second arms.

Barbera-Guillem et al. teach a method for detecting a specific nucleic acid in a target sample using a molecular probe having a capture reagent comprising a plurality of first arms (primary dots with plurality of polynucleotide strands) and a plurality of second arms (secondary dots with plurality of polynucleotide strands), wherein the second arms are complementary to the capture sequence of the first component forming a dendrimer of multiple layer , thereby resulting a detectable signal and an exponential increase in the amount of detectable signal that can be detected from a single molecular probe (see col. 2, line 13-46).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method for determining the presence of a specific nucleotide sequence as taught by Dellinger et al. with a molecular probe comprising multiple first and second arms as taught by Barbera-Guillem et al. to achieve expected advantage of amplifying the detectable signal from a single molecular probe in detecting a target nucleic acid. An ordinary practitioner would have been motivated to combine the method of Dellinger et al. with the step of adding a molecular probe comprising multiple first and second arms as taught by Barbera-Guillem et al. for the purpose of amplifying the detectable signal and increasing the specificity and sensitivity of detecting a target nucleic acid. An ordinary person skilled in the art would have a reasonable expectation of success that such modification would result in reducing non-specific binding and reduce background noise and enhance specific hybridization signal because Barbera-Guillèm et al. explicitly taught that the use of a molecular probe having a capture reagent comprising a plurality of first arms (primary dots with plurality of polynucleotide

strands) and a plurality of second arms (secondary dots with plurality of polynucleotide strands), wherein the second arms are complementary to the capture sequence of the first component forming a dendrimer of multiple layer , thereby resulting a detectable signal and an exponential increase in the amount of detectable signal that can be detected from a single molecular probe (see col. 2, line 13-46).Such modification is considered as obvious over the cited prior art in the absence of secondary considerations.

B. Claims 18, 35, 37-38, 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dellinger et al. (USPN. 5, 853,993) in view of Barbera-Guillem et al. (US 6,261,779) as applied to claims 1-3, 7-8, 17, 19-21, 22, 25-26, 36, 39-54, 56 above, and further in view of Weston et al (WO99/37805, 29 July 1999).

Dellinger et al. in view of Barbera-Guillem et al. teach a method for determining the presence of a specific nucleotide sequence as discussed above in section 5A.

However, neither Dellinger et al. nor Barbera-Guillem et al. teach use of blocker probes comprising locked nucleic acid nucleotide (LNA).

Weston et al. teach a method of claims 18, 35, detecting a nucleotide sequence of interest comprising a target DNA and a blocking oligonucleotide that hybridizes to the sequence of interest to inhibit re-annealing of the target strand to its complementary strand (see page 11, paragraph 1).

With regard to claim 37-38, 55, Weston et al. teach the blocking oligonucleotide comprises LNA, PNA, DNA or combination thereof. (see page 11, paragraph 1).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method for determining the presence of a specific

nucleotide sequence as taught by Dellinger et al. in view of Barbera-Guillem et al. with a blocker probe comprising LNA probe as taught by Weston et al. to achieve expected advantage of developing an enhanced sensitivity of detecting a target nucleic acid. An ordinary practitioner would have been motivated to combine the method of Dellinger et al. in view of Barbera-Guillem et al. with the step of adding blocker probe as taught by Weston et al. for the purpose of reducing the background noise increasing the specificity and sensitivity of detecting a target nucleic acid. An ordinary person skilled in the art would have a reasonable expectation of success that such modification would result in reducing non-specific binding and reduce background noise and enhance specific hybridization signal because Weston et al. taught that the use of blocker probe in hybridization assays allow specific and efficient hybridization and minimizes the reannealing of the target strand to its complementary strand thereby reduces non-specific (back-ground noise) hybridization (page 11, line 9-13 of paragraph 1) and such modification is considered as obvious over the cited prior art.

C. Claims 4-6, 9-16, 23-24, 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dellinger et al. (USPN. 5, 853,993) in view of Barbera-Guillem et al. (US 6,261,779) as applied to claims 1-3, 7-8, 17, 19-21, 22, 25-26, 36, 39-54, 56 above, and further in view of Van Ness et al. (USPN. 6,361,940).

Dellinger et al. in view of Barbera-Guillem et al. teach a method for determining the presence of a specific nucleotide sequence as discussed above in section 5A.

However, neither Dellinger et al. nor Barbera-Guillem et al. teach hybridization temperatures ranging from 50-60^0 C, incubation time, and base solution to separate and purge the hybridized RNA reagent.

Van Ness et al. teach a method for enhancing hybridization and probing or priming specificity, wherein Van Ness et al. teach parameters of a thermal melting profiles (helical coil transition) of an oligonucleotide in hybridization solutions (hybotropic or salt solutions used for separating and purging of hybridized complexes from an array) and the dependency of temperatures (discrimination temperatures) based on the base composition and G-C content of the oligonucleotide probes ranging from 0- 80^0 C (see col. 34, line 48-67, col. 35, line 1-45, col. 45, line 4-33). With regard to claims 4, 6, 22, 24, Van Ness et al. also teach the base solution is sodium hydroxide (see col. 66, line 10-14); With regard to claims 13, 15, 29, 31, Van Ness et al. teach that the probe nucleotide sequences on microarray comprise oligonucleotides and cDNA sequences (see col. 66, line 21-40).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method for determining the presence of a specific nucleotide sequence as taught by Dellinger et al. in view of Barbera-Guillem et al. with a the parameters that enhance hybridization specificity such as incubation temperatures and hybridization solutions as taught by Van Ness et al. to achieve expected advantage of developing an enhanced sensitivity and specificity of detecting a target nucleic acid. An ordinary practitioner would have been motivated to combine the method of Dellinger et al. in view of Barbera-Guillem et al. with the step of adding said hybridization parameters as taught by Van Ness et al. for the purpose of increasing the specificity of hybridization assay. An ordinary person skilled in the art would have a reasonable expectation of success that such modification would result in enhance specificity of hybridization signal because Van Ness et al. explicitly taught that the parameters to optimize hybridization conditions and to increase hybridization

specificity (col. 56, line 52-67, col. 57, line 1-16) and such modification is considered as obvious over the cited prior art. Further, selection of specific hybridization conditions including incubation time, temperatures, oligonucleotide probes represents routine optimization with regard to sequence, length and composition of the oligonucleotide, which routine optimization parameters are explicitly recognized in Van Ness et al. As noted in *In re Aller*, 105 USPQ 233 at 235,More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Routine optimization is not considered inventive and no evidence has been presented that the selection of hybridization conditions performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

D. Claim 57 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dellinger et al. (USPN. 5, 853,993) in view of Barbera-Guillem et al. (US 6,261,779) as applied to claims 1-3, 7-8, 17, 19-21, 22, 25-26, 36, 39-54, 56 above, and further in view of Coutlee et al. (J Clin Microbiol., Vol. 27, No. 5, pp. 1002-1007, 1989).

Dellinger et al. in view of Barbera-Guillem et al. teach a method for determining the presence of a specific nucleotide sequence as discussed above in section 5A.

However, neither Dellinger et al. nor Barbera-Guillem et al. teach use of a ribonuclease inhibitor to protect said RNA reagent.

Coutlee et al. teach a method for detecting DNA-RNA hybrids, wherein Coutlee et al. teach the use of a ribonuclease inhibitor to protect RNA reagent (see page 1003, col. 1, line 8-13, paragraph 1).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method for determining the presence of a specific nucleotide sequence as taught by Dellinger et al. in view of Barbera-Guillem et al. with a ribonuclease inhibitor as taught by Coutlee et al. to achieve expected advantage of developing an enhanced sensitivity and specificity of detecting a target nucleic acid. An ordinary practitioner would have been motivated to combine the method of Dellinger et al. in view of Barbera-Guillem et al. with the step of adding said ribonuclease inhibitor as taught by Coutlee et al. because an ordinary person skilled in the art would have a reasonable expectation of success that the combination would result in protecting RNA reagent because Coutlee et al. explicitly taught that the use of said ribonuclease inhibitor in hybridization to increase the detection of stable RNA-DNA hybrids (see page 1003, col. 1, line 8-13, paragraph 1) and such modification is considered as obvious over the cited prior art.

E. Claim 58 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dellinger et al. (USPN. 5, 853,993) in view of Barbera-Guillem et al. (US 6,261,779) as applied to claims 1-3, 7-8, 17, 19-21, 22, 25-26, 36, 39-54, 56 above, and further in view of Knight et al. (US 4,753,530).

Dellinger et al. in view of Barbera-Guillem et al. teach a method for determining the presence of a specific nucleotide sequence as discussed above in section 5A.

However, neither Dellinger et al. nor Barbera-Guillem et al. teach a dual channel analysis.

Knight et al. teach a multichannel analysis system to enhance detection of a target with low signal intensities in situ, wherein Knight et al. teach that the system comprises a multi channel optical probe for analysis of a target (see col. 2, line 63-67, col. 3, line 21-40).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method for determining the presence of a specific nucleotide sequence as taught by Dellinger et al. in view of Barbera-Guillem et al. with a a step of dual channel analysis as taught by Knight et al. to achieve expected advantage of developing an enhanced sensitivity and specificity of detecting a target nucleic acid. An ordinary practitioner would have been motivated to combine the method of Dellinger et al. in view of Barbera-Guillem et al. with the step of dual channel analysis as taught by Knight et al. because an ordinary person skilled in the art would have a reasonable expectation of success that the combination would result in protecting RNA reagent because Knight et al. explicitly taught that the use of a multichannel analysis would increase the detection of a target with low signal intensities , even in the presence of dark current or sunlight (see col. 2, line 63-67, col. 2, line 21-40) and such modification is considered as obvious over the cited prior art.

Response to arguments:

6. With regard to the rejection of claims 1-3, 7-8, 17, 19-22, 25-26, 36 and 39-56 under 35 USC 103(a) as being obvious over Dellinger et al. in view of Barbera-Guillem, Applicants' arguments are fully considered and found unpersuasive. Applicants argue that neither of the references teach or could be used to directly assay RNA as required by the claims. The references use cDNA due to the unstability of RNA and the present invention overcomes the stability issues and uses RNA directly. Applicants' arguments are fully considered and found not persuasive. The

instant claims recite "RNA reagent" and the instant specification does not define RNA reagent as RNA. Thus thus the RNA reagent as recited in the claims do not necessarily read only on RNA, rather it can also read on cDNA. Thus the scope of the instant claims do not exclude cDNA. Thus the arguments based on the direct use of RNA is not persuasive.

Further Applicants argue that the references do not teach direct RNA system and the Barbara –Guillem itself admits the disadvantages and the stability problems of quantum dots and argue that there is no teaching or suggestion in the references together or alone to combine or modify the method , except for hindsight. The arguments based on the RNA stability issues are fully considered however as discussed above the instant claims do not exclude cDNA as a RNA reagent and is within the scope of the claims as presented. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case Barbara-Guillem et al. does provide a motivation to use the multiple arm quantum dots to increase the signal as discussed in the rejection and it would have been obvious to modify the method of Dellinger et al. in a manner taught by Barbara-Guillem et al. as discussed in the rejection to achieve the expected advantage.

With regard to no teaching or suggestion to combine the references, examiner notes that obviousness can only be established by combining or modifying the teachings of the prior

art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in thereferences themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In this case, specific motivation is provided in the rejection, which states that An ordinary person skilled in the art would have a reasonable expectation of success that such modification would result in reducing non-specific binding and reduce background noise and enhance specific hybridization signal because Barbera-Guillem et al. explicitly taught that the use of a molecular probe having a capture reagent comprising a plurality of first arms (primary dots with plurality of polynucleotide strands) and a plurality of second arms (secondary dots with plurality of polynucleotide strands), wherein the second arms are complementary to the capture sequence of the first component forming a dendrimer of multiple layer , thereby resulting a detectable signal and an exponential increase in the amount of detectable signal that can be detected from a single molecular probe (see col. 2, line 13-46) and such modification is considered as obvious over the cited prior art.

Applicants further argue that the new claims 57 and 58 recite the use of a ribonuclease inhibitor and dual channel assay which are not taught or suggested by the references on record. The new claims added herein are not yet examined and therefore the arguments are not persuasive.

7. With regard to the rejection of claims 18, 35, 37-38 under 103(a) as being obvious over Dellinger et al. in view of Barbara-Guillem et al. further in view of Weston, Applicants' arguments are fully considered and found unpersuasive. Applicant argue that Weston teaches use of blocking oligonucleotides to prevent re-annealing of a target strand with its complementary

strand and the present invention does not use blocking agents to prevent re-annealing and there would be no reason for one of the ordinary skill to look to Weston. Applicants also argue that the Weston does not teach use of an LNA as a part of the capture sequence and does not teach use of blocking nucleic acids or LNA as they are used in the instant invention. Applicants' arguments are found unpersuasive because as noted in MPEP 2144 (R-5) The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. >See, e.g., In re Kahn, 441 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). There is no requirement that the prior art provide the same reason as the applicant to make the claimed invention. Further Weston et al. does teach blocking nucleic acids or LNA as discussed in the rejection above. The rejection is maintained.

8. With regard to the rejection of claims 4-6, 9-16, 23-24, 27-34 under 35 USC 103(a) as being obvious over Dellinger et al. in view of Barabara-Guillem et al. further in view of Van Ness et al., Applicants did not provide any arguments and the rejection is maintained herein.

9. With regard to the double patenting rejections Applicants arguments are considered and the rejections are maintained herein since the scope of the co-pending claims remain within the scope of the instant claims.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Suryaprabha Chunduru
Primary Examiner
Art Unit 1637.

Prabha Chunduru 4/26/07
SURYAPRABHA CHUNDURU
PRIMARY EXAMINER